REMARKS

Claims 51-59 were pending in the application. In the instant Amendment, claims 51-52, 54-55, 56, and 58-59 have been amended to clarify the invention. Upon entry of the above-made amendments, claims 51-59 will be pending.

Claim 51 has been amended to clarify that step (2) determines statistical significance of said similarity between said *determined* interpolated response profile and said diagnostic profile such that the claim step has proper antecedent basis (emphasis added). Claim 51 has also been amended to recite in the last line of step (1) that the level of disease state "correlated to said determined interpolated response profile indicates said level of said disease state *of said subject*" (emphasis added). Claim 51 has further been amended to recite in step (3) that said patient is diagnosed as "having said level of said disease *correlated to said determined interpolated response profile* if said statistical significance is at least 95%" (emphasis added). These amendments are intended to make the claim language clearer. Claim 51 has also been amended to delete the recitation "said level of said disease state in said subject by a method comprising determining" from the first and second lines of step (1) to make the claim language more concise.

Claims 52 and 56 have been amended to recite that said *determined* interpolated response profile yields a maximum correlation (claim 52) or a minimum difference (claim 56) between said diagnostic profile and said *determined* interpolated response profile such that the claims have proper antecedent basis (emphasis added).

Claims 54-55 and 58-59 have been amended by replacing the numerical designation of claim steps with alphabetical designation so that the steps in these claims are distinguishably designated in view of those of the base claim.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

APPLICANTS' INTERVIEW SUMMARY

Applicants thank Examiner Ardin Marschel, Ph.D., for the courtesies extended during the telephone interview on April 27, 2004 (hereinafter "the Interview") with Applicants' representatives Adriane M. Antler, Ph.D., and Weining Wang, Ph.D. During the interview, the claim rejection under 35 U.S.C. § 112, second paragraph, and the claim rejection under 35 U.S.C. § 102 (b) and (e)(2) based on Swift et al., U.S. Patent No. 5,464,742 ("Swift"), or,

in the alternative, under 35 U.S.C. § 102(e)(2) based on Anderson et al., U.S. Patent No. 6,267,722 ("Anderson"), were discussed.

With respect to the rejection under 35 U.S.C. § 112, second paragraph, Dr. Antler first pointed out that the meaning of the word "interpolation" is commonly known in the art. As an example, Dr. Antler directed the Examiner's attention to a definition given by the Free On-line Dictionary of Computing as obtained from the web site of Dictionary.com at http://dictionary.reference.com/search?q=INTERPOLATION, where "interpolation" is defined as "[a] mathematical procedure which estimates values of a function at positions between listed or given values. Interpolation works by fitting a 'curve' (i.e. a function) to two or more given points and then applying this function to the required input." The invention as reflected by the language of the claims was then discussed. The Examiner agreed that since Applicants were relying on an art-accepted definition of "interpolation," the rejection should be withdrawn.

With respect to the rejection under 35 U.S.C. § 102 (b) and (e)(2) based on Swift, Dr. Antler pointed out that Swift teaches a process for testing the association between an allele and a disease. Dr. Antler also pointed out that even if assuming, *arguendo*, that, as the Examiner contends, "homozygous normal," "homozygous abnormal," and "heterozygous" are different "levels" of a disease, such levels cannot be interpolated since interpolated values, e.g., intermediate values of these "levels," do not make sense and would not correspond to any disease levels, and, indeed, such levels are not interpolated in Swift. Swift does not teach interpolating response profiles, each of which corresponds to a level of a disease, to obtain interpolated response profiles. Nor does Swift teach determining a level of a disease by determining the interpolated profile which has the greatest similarity to a diagnostic profile. The Examiner indicated that in view of Dr. Antler's explanation, the rejection based on Swift would be withdrawn.

With respect to the rejection under 35 U.S.C. § 102 (e)(2) based on Anderson, Dr. Antler pointed out that, in Anderson, curve fitting algorithms are used for image processing, e.g., to generate parameters to define the obtained image. Dr. Antler directed the Examiner's attention to Anderson, columns 23-24, which presents the details of the "curve fitting" mentioned in col. 2, lines 59 and 66-67 of Anderson, for a description of curve fitting as used in Anderson. As the cited description shows, in Anderson, curve fitting is carried out on

features in an acquired image of reflectance data (see col. 23, lines 23 to col. 24, line 1). Dr. Antler explained that even assuming, *arguendo*, that the image features represent meausrements of cellular constituents, the curve fitting is performed on measurements of the different cellular constituents measured in the assay, rather than on measurements of a single cellular constituent over a plurality of different disease levels. Dr. Antler also explained that even assuming, *arguendo*, that the curve fitting in Anderson qualifies as interpolation, the interpolation in Anderson is not performed on measurements of an individual cellular constituent, and is not performed over different levels of a disease. In contrast, in the presently claimed invention, claim 51 part (ii) specifies that the interpolation is performed on measurements of "each said cellular constituent ... over said plurality of levels of said disease state." Dr. Antler then explained that, in Anderson, diagnosis is carried out based on the parameters generated in the image processing step, as described in Anderson, starting at column 28. Thus, Anderson does not teach determining a level of a disease by determining the interpolated profile which has the greatest similarity to a diagnostic profile. The Examiner indicated that he wished to further review Anderson.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 51-59 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner contends that the meaning of interpolation in the claimed method is unclear. As discussed above, the meaning of the word "interpolation" as used in the presently claim invention is its meaning commonly known in the art. As an example, "interpolation" may be defined as "[a] mathematical procedure which estimates values of a function at positions between listed or given values. Interpolation works by fitting a 'curve' (i.e. a function) to two or more given points and then applying this function to the required input" (see the definition provided by the Free On-line Dictionary of Computing as cited on the bottom of page 2 through the top of page 3 of a printout of the web page at http://dictionary.reference.com/search?q=INTERPOLATION, attached herewith as Exhibit A). The claim language with respect to interpolation practice is therefore clear, and the rejection should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 51-53, 56 and 57 are rejected under 35 U.S.C. § 102(b) and (e)(2) as being anticipated by Swift et al., U.S. Patent No. 5,464,742 ("Swift"), or, in the alternative, under 35 U.S.C. § 102(e)(2) by Anderson et al., U.S. Patent No. 6,267,722 ("Anderson"). Applicants respectfully disagree with the Examiner for the reasons presented below.

A claim is anticipated under 35 U.S.C. § 102 only if each and every element and limitation as set forth in the claim is found, either expressly described or inherently present, in a single prior art reference. *Glaxo, Inc. v. Novopharm Ltd.,* 52. F.3d 1043, 1047 (Fed. Cir. 1995). There must be *no differences* between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991). Anticipation requires that all aspects of the claimed invention were already described in a *single* reference. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991).

The presently claimed invention provides a method for diagnosing a level of a disease state of a subject. The claimed method comprises determining an interpolated response profile that best fits a diagnostic profile (i.e., similarity is the greatest between the determined interpolated response profile and the diagnostic profile). The diagnostic profile comprises measurements of a first plurality of cellular constituents in one or more cells of the subject. The interpolated response profile determined in step (1) (i.e., the "determined interpolated response profile") comprises measurements of a second plurality of cellular constituents, each of which is extracted from an interpolated response curve of measurements of a respective cellular constituent as a function of the level of the disease state. The interpolated response curve of each such cellular constituent is obtained using measurements of the respective cellular constituent contained in a set of provided response profiles, each provided response profile comprising measurements of the second plurality of cellular constituents in one or more cells of an analogous subject at one of a plurality of levels of the disease, by interpolating such measurements of the respective cellular constituent over the plurality of levels of the disease. Thus, measurements of a cellular constituent contained in different provided response profiles are interpolated over the plurality of levels of the disease to generate an interpolated response curve. Once the interpolated response profile that has the greatest similarity to the diagnostic profile is determined, the level of the disease state

corresponding to the determined interpolated response profile is taken as the level of the disease state of the subject. The statistical significance of the similarity between the determined interpolated response profile and the diagnostic profile is then determined in step (2) of the method. The subject is diagnosed in step (3) of the method as having the level of the disease as represented by the determined interpolated response profile if the statistical significance is greater than 95%.

Swift teaches a process for testing the association between an allele and a disease. The process involves a comparison of the proportion of test individuals who have the disease and carry the allele from a set of families in which the allele is present and the proportion of test individuals expected to carry the allele if there is no association between the allele and the disease. As discussed during the Interview, even if assuming, *arguendo*, that, as the Examiner contends, "homozygous normal," "homozygous abnormal," and "heterozygous" are different "levels" of a disease, such levels cannot be interpolated since interpolated values, e.g., intermediate values of these "levels," do not make sense and would not correspond to any disease levels, and, indeed, such levels are not interpolated in Swift. Swift does not teach interpolating response profiles, each of which corresponds to a level of a disease, to obtain interpolated response profiles. Nor does Swift teach determining a level of a disease by determining the interpolated profile which has the greatest similarity to a diagnostic profile.

Anderson teaches systems and methods of measuring and analyzing diagnostic tests and assays for diagnosis or risk assessment for patients. In Anderson, diagnostic data are measured using an appropriate test or assay, such as an immunoassay. The measured data are then processed employing data reduction and curve fitting algorithms for accurately determining the presence or concentration of the tested substance (see, e.g., Anderson, column 2, lines 55-62). Thus, as discussed in the Interview, in Anderson, curve fitting algorithms are used for image processing, e.g., to generate parameters to define the obtained image (see, e.g., columns 23-24 of Anderson, which presents the details of the "curve fitting" mentioned in col. 2, lines 59 and 66-67 of Anderson, for a description of curve fitting as used in Anderson). As the cited description shows, in Anderson, curve fitting is carried out on features in an acquired image of reflectance data (see col. 23, lines 23 to col. 24, line 1). Even assuming, *arguendo*, that the image features represent measurements of cellular constituents, the curve fitting is performed on measurements of the different cellular

constituents measured in the assay, rather than on measurements of a single cellular constituent over a plurality of different disease levels. Even assuming, *arguendo*, that the curve fitting in Anderson qualifies as interpolation, the interpolation in Anderson is not performed on measurements of an individual cellular constituent, and is not performed over different levels of a disease. In contrast, in the presently claimed invention, claim 51 part (ii) specifies that the interpolation is performed on measurements of "each said cellular constituent ... over said plurality of levels of said disease state." Furthermore, in Anderson, diagnosis is carried out based on the parameters generated in the image processing step. For example, Anderson teaches classifying an image based on the generated parameters by comparing the generated parameters to relevant reference data (Anderson, column 28, line 39, through column 30, line 5) or by a neural network approach (Anderson, column 30, line 6, through column 31, line 33). Thus, Anderson does not teach determining a level of a disease by determining the interpolated profile which has the greatest similarity to a diagnostic profile.

Therefore, Applicants respectfully submit that neither Swift nor Anderson anticipate claims 51-53, 56 and 57, and that the rejection under U.S.C. § 102(b) and (e)(2) based on Swift and the rejection under U.S.C. § 102(e)(2) based on Anderson should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

Date: May 4, 2004

32,605

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6 entries found for *INTERPOLATION.*

in·ter·po·late Pronunciation Key (ĭn-tûr′pə-lāt′)
v. **in·ter·po·lat·ed, in·ter·po·lat·ing, in·ter·po·lates**
v. tr.

1. To insert or introduce between other elements or parts.
2. a. To insert (material) into a text.
   b. To insert into a conversation. See Synonyms at introduce.
3. To change or falsify (a text) by introducing new or incorrect material.
4. *Mathematics.* To estimate a value of (a function or series) between two known values.

v. intr.

To make insertions or additions.

[Latin interpolāre, interpolāt-, *to touch up, refurbish,* from interpolis, *refurbished.* See pel-[5] in Indo-European Roots.]

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in·ter′po·la′tion *n.*
in·ter′po·la′tive *adj.*

in·ter'po·la'tor *n.*

[Download or Buy Now]
Source: *The American Heritage® Dictionary of the English Language, Fourth Edition*

INTERPOLATION

\In*ter`po*la"tion\, n. [L. interpolatio an alteration made here and there: cf. F. interpolation.] 1. The act of introducing or inserting anything, especially that which is spurious or foreign.

2. That which is introduced or inserted, especially something foreign or spurious.

Bentley wrote a letter . . . . upon the scriptural glosses in our present copies of Hesychius, which he considered interpolations from a later hand. --De Quincey.

3. (Math.) The method or operation of finding from a few given terms of a series, as of numbers or observations, other intermediate terms in conformity with the law of the series.

Source: *Webster's Revised Unabridged Dictionary, © 1996, 1998 MICRA, Inc.*

INTERPOLATION

n 1: (mathematics) calculation of the value of a function between the values already known 2: an action or remark that interrupts [syn: interjection, interposition]

Source: *WordNet ® 1.6, © 1997 Princeton University*

INTERPOLATION

<mathematics, algorithm> A mathematical procedure which estimates values of a function at positions between listed or given values. Interpolation works by fitting a "curve" (i.e. a function) to two or more given points and then applying this function to the required input. Example uses are calculating trigonometric functions from tables and

audio waveform sythesis.

The simplest form of interpolation is where a function, f(x), is estimated by drawing a straight line ("linear interpolation") between the nearest given points on either side of the required input value:

$f(x) \sim f(x1) + (f(x2) - f(x1))(x-x1)/(x2 - x1)$

There are many variations using more than two points or higher
degree polynomial functions. The technique can also be extended to functions of more than one input.

(1997-07-14)

Source: *The Free On-line Dictionary of Computing, © 1993-2003 Denis Howe*

INTERPOLATION

interpolation in InvestorWords

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INTERPOLATION

interpolation: in CancerWEB's On-line Medical Dictionary

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antonyms